UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,700	10/15/2004	Monica Petronella Maria De Maat	101137-56	2836

27387 7590 04/25/2007

NORRIS, MCLAUGHLIN & MARCUS, P.A.
875 THIRD AVE
18TH FLOOR
NEW YORK, NY 10022

EXAMINER	
SAUCIER, SANDRA E	
ART UNIT	**PAPER NUMBER**
1651	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/25/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,700	DE MAAT ET AL.	
	Examiner	Art Unit	
	Sandra Saucier	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-4,6 and 9-35* is/are pending in the application.

4a) Of the above claim(s) *10 and 14-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-4,6,9,11-13 and 25-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *15 October 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 2-4, 6, 9-35 are pending. Claims 2-4, 6, 9, 11-13, 25-35 are considered on the merits. Claims 10, 14-24 are withdrawn from consideration as being drawn to a non-elected invention.

Election/Restriction

Applicant's election of Group I in the reply filed on 3/2/07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

Specification

The disclosure is objected to because of the following informalities: The specification on page 3 states that a healthy person (normal blood) has about 5% of total circulating fibrinogen of the Fib420 variety. On page 4, it is stated that in blood of healthy persons, about 70% is in the HMW form (340kDa), 26% in LMW form (305kDa), and 4% in LMW' form (270kDa). This adds up to 100%, but the statements are contradictory because 5% should be in Fib420 form, but this 5% is not accounted for in the total fibrinogen content of blood of a normal person. Appropriate clarification is required.

Claim Rejections - 35 USC § 112

SCOPE of ENABLEMENT

Claims 2-4, 6, 9, 11-13, 25-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an *in vitro* method for modifying the properties of a fibrin matrix, does not reasonably provide enablement for an *in vivo* method, specifically claimed in claims 11-13, 35. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The application states, "To date the enzyme which converts HMW to LMW and LMW' has not been identified" (page 4). This is a statement with regard to the state of the art at the time of invention. If the enzyme which converts one form of fibrinogen to another is not even known, it follows that how to vary the activity of an unknown enzyme *in vivo* in order to *modify* the concentration of circulating variants of fibrinogen is also unknown. Therefore, manipulation of the forms of fibrinogen *in vivo* is not enabled. Nor does the prior art provide for any such manipulations *in vivo*. Further, no exemplification is given to show such an *in vivo* treatment. Thus, neither the specification nor the prior art provides enablement for the claimed method *in vivo*.

Claim 12 recites that the composition is applied to inhibit or prevent tumor growth. The prior art teaches that the presence of a fibrin matrix, protects tumors from destruction by cytotoxic cells (Gunji *et al.* [U]), and prevention of fibrin matrix formation enhances the cytotoxic destruction of tumor cells, (Vaage *et al.* [V],) and that fibrin coagulation prevents induction of LAK activity (Atagi *et al.* [W]). Thus, the prior art does not support the claimed method, nor is the claimed method shown in a working example in the specification. Thus, the claimed method is not enabled.

Undue experimentation would be required to practice the invention as claimed due to the amount of experimentation necessary because of the limited amount of guidance and limited number of working examples in the specification, the nature of the invention, the state of the prior art, breadth of the claims and the unpredictability of the art.

As set forth in *In re Fisher*, 427 F2.d 833, 839, 166 USPQ 18, 24 (CCPA) 1970: [Section 112] requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.

In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of the enablement varies inversely with the

degree of unpredictability of the factors involved. *Ex parte Humphreys*, 24 USPQ2d, 1260.

Please amend the independent claim to recite *"in vitro"* and cancel claims 11-13 and 35 which will overcome the enablement rejection.

INDEFINITE

Claims 2-4, 6, 9, 11-13, 25-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite because they depend on a varying composition of fibrinogen variants as the starting material. A claim may be rendered indefinite by reference to an object that is variable. For example, the Board has held that a limitation in a claim to a bicycle that recited "said from and rear wheels so spaced as to give a wheelbase that is between 58 and 75 percent of the height of the rider that the bicycle was designed for" was indefinite because the relationship of parts was not based on any known standard for sizing a bicycle to a rider, but on a rider of unspecified build. *Ex parte Brummer*, 12 USPQ2d 1653 (Bd. Pat. App. & Inter. 1989).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action: A person shall be entitled to a patent unless (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent, (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 2-4, 6, 9, 25-34 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by WO 00/62833 [N] or US 6,946,140 [A] or Holm *et al.* [X] or Hasegawa *et al.* [U2], Smith *et al.* [V2] or Falls *et al.* [W2].

The claims are directed to a method comprising:

a) selecting a composition consisting of multiple variants of fibrinogen (of which one is HMW fibrinogen),
b) modifying the fibrinogen to change the relative concentration of at least one variant, and
c) forming a fibrin matrix from the composition of step b).

Since applicant states the response to the restriction requirement that there is HMW in some amount in all the elected claim methods, a change in any concentration of any variant will necessarily cause a change in the relative concentration of the HMW variant.

The references are relied upon as explained below.

WO 00/62833 discloses in Example 1, page 29, normal plasma which contains a mixture of fibrinogen types, precipitation by glycine, precipitation by ammonium sulfate 25% saturation which produces a purified fibrinogen with a mixture of types as evidence by fibrinogen bands I and II.

Also fractions (Sample 2) were produced from a mixture of fibrinogen types which had "all its alpha chains intact, but lacked molecules with gamma chains that have an extended carboxy terminal which constitutes approximately 15% of the fibrinogen in plasma. Another fraction was produced which had all alpha chains intact and contained molecules with both extended and non-extended gamma chains.

Also, Sample 4 contain 20-30% of molecules with degraded alpha chains. Other fractions were also produced with changes in the relative concentration of fibrinogen variants. Sample 4 was clottable.

US 6,946,140 also fractionates fibrinogen ppt. from normal plasma and produces fibrin gels from the various fractions and tests the gels for fibroblast migration activity. See Examples 1 and 2.

Holm *et al.* discloses a method comprising :
selecting "normal" fibrinogen, fractionating to form fractions with more or less HMW, LMW and LMW' than the "normal" distribution (Fig 2), forming a fibrin matrix (clot) (page 171).

Hasegawa *et al.* disclose fractionating fibrinogen into fractions F1 and F2 with molecular weights of 340 and 325kDa (page 184), forming a fibrin clot (Fig. 2).

Smith *et al.* disclose producing mixtures of fibrinogen variants from purified variants (page 22081) and forming fibrin clots (Fig. 2).

Falls *et al.* disclose purifying fibrinogen to form fractions with different ratios of fibrinogen variants (p. 14252), forming fibrin clots.

Although the types of fibrinogen in the composition of the prior art are not always expressed in the same way as in the claimed method, and because the concentrations in the claims are expressed as relative concentrations, in the absence of evidence to the contrary, the method of the references is deemed to fall within the claim limitations because a permutation in any variant concentration will cause a relative variation in all other variants in the composition. Clarification of the invention and claim language may serve to advance prosecution.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action: (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2-4, 6, 9, 11-13, 25-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/62833 [N] or US 6,946,140 [A] or Holm *et al.* [X] or Hasegawa *et al.* [U2], Smith *et al.* [V2] or Falls *et al.* [W2].

The claims were discussed above.

To the extent that the claims can be interpreted, the references are applied as explained above. Further, claims 2 and 6 merely recite desired results and as such are also rejected over the references of record.

One of ordinary skill in the art would have been motivated at the time of invention to produce this composition in order to obtain the results as suggested by the references with a reasonable expectation of success. The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

Conclusion

Applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). It is applicants' burden to indicate how amendments are supported by the ORIGINAL disclosure. Due to the procedure outlined in MPEP 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 USC 102 or 35 USC 103(a) once the aforementioned issue(s) is/are addressed.

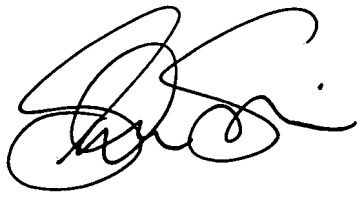
Applicant is requested to provide a list of all copending applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to the office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone

number is (571) 272-0922. The examiner can normally be reached on Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, M. Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Sandra Saucier
Primary Examiner
Art Unit 1651
April 23, 2007